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För Patent- och registreringsverket
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APPARATUS AND METHOD FOR ANALYSING

Technical field of the invention

The present invention relates to a sample presentation apparatus for use in analysing pharmaceutical products, for example solid dosage forms such as a tablet, a pellet or a capsule. The invention further relates to a method for presentation of samples to an analysing equipment.

Background of the invention

Non-invasive, non-destructible analysis of whole tablets can be carried out by means of near-infrared (NIR) or Raman spectrometry. The common feature of both these techniques is that they utilise light in the NIR wavelength region (700-2500 nm, specifically 700-1500 nm) where pharmaceutical tablets generally are relatively transparent (low molar absorptivity). Thus, light can in this region penetrate by several millimeters compressed powders and tablets and information on the content can be obtained emanating from the inside of the tablet and not only from the surface.

Typically, tablet analysers acquire a spectrum for each tablet when the sample is positioned in the measuring light beam. A tablet is presented to the analysing beam by a sample holding device, e.g. a holder for a single tablet or for a plurality of tablets so as to perform a plurality of spectrometric measurements. Measurements on a solid dosage form such as a tablet, a pellet or a capsule, are conducted to obtain information for example on the concentration of the active drug and/or the concentration of non-active components or their spatial distribution, i.e. homogeneity. In particular, it is of interest to monitor the quality consistency of doses during the manufacturing process. Thus, real-time measurements during the manufacturing process, for example during the tabletting process, may reveal important information to be used for controlling the process.

G01N 21/35, 33/15

EP 0767 369 A discloses an apparatus for NIR transmission measurements of tablets containing pharmaceutical compounds. An object of this apparatus is to minimise or

eliminate the incidence of stray light reaching the detector and therefore, a sample locator is used together with a masking device. The sample, a tablet, is positioned in a cylindrical well within the locator and thereafter an annular masking element is placed within the well to engage the top surface of the tablet. In this way the possibility that light will leak around the sample is minimised. The sample locator could either comprise only one well for performing a single tablet analysis or several wells disposed on a rotating plate in the case of performing a plurality of tablet analyses.

In the above described prior art with a device having a sample locator comprising one well, only one tablet can be analysed at a time. The insertion of the tablet into the well is manually performed as well as the positioning of the locator into the analysing position. However, with the sample locator comprising several wells, a predetermined number of tablets can be analysed in sequence. In the latter alternative, a limited set of tablets can be analysed in sequence. However, insertion of the tablets into each well still has to be done manually prior to the automated analysis. Therefore, the number of analyses is limited to the number of wells in the sample locator, which omits its use for continuous automated analysis. A further drawback is that the bottom aperture of each well containing the tablet, i.e. the opening closest to the detector, thus constitutes the active aperture during the spectrometric analysis. Accordingly, this inevitably results in a large number of apertures, i.e. the number of wells in the sample locator, used in the analysis performed. As the physical dimensions and surface finish of each well may not be truly identical, this will introduce imprecision in the analysis.

B07C 5/34, 5/342, G01N 21/25, B65G 47/14
DE 4441686 A relates to an apparatus for testing tablets. From a batch source containing tablets to be tested, tablets are transported via a vibrating table down to a sloping table from which the tablets fall into a feeder wheel positioned just above a rotating testing plate comprising drilled holes to receive tablets. The feeder wheel continuously drops one tablet into each hole on the rotating testing plate. The tablets are exposed to a light beam from a light source hanging above the testing plate and a detector is placed under the testing plate.

In this prior art device a continuously automated analysis can be performed. However, for each tablet there will be a new aperture presented to the measuring device and as mentioned above a large number of apertures will introduce imprecision in the analysis. Further, vibrations from the vibrating table is likely to effect the rotating test plate. These vibrations will disturb the on-going measurements.

None of the mentioned prior art documents describe an apparatus suitable for presenting a sample to a spectrometric imaging measurement system.

Summary of the invention

The object of the present invention is to solve or alleviate some or all of the problems described above. More specifically, the apparatus and method according to the invention should allow for performance of a measurement(s) on a pharmaceutical sample with high accuracy, precision and reliability.

A further object of the invention is to perform continuous and automated measurements of pharmaceutical samples preferably connected on-line to a tabletting process.

According to a first embodiment of the present invention there is provided a sample presentation apparatus for use in analysing pharmaceutical samples, comprising means for feeding said samples sequentially through a sample presentation unit comprising at least one predetermined analysing position wherein at least one measuring radiation beam irradiates on said sample when located in said analysing position characterised by at least one two-piece means for temporarily fixing each sample at said analysing position, said two-piece means comprising a first and a second sample holding part arranged at said analysing position in which said two-piece means is adapted to move between

- a resting position wherein a sample is provided for analyse, and
- a fixing position wherein a sample is analysed.

The present invention provides for an automated and continuous analysis of samples on-line, from for example a tabletting process, or at-line from for example a batch source of tablets. In contrast to prior art techniques the present invention provides an apparatus for fast and reliable measurements in which there is no need for manual handling of the samples.

The alignment of each sample to be analysed is optimised with respect to achieving high reproducibility of positioning the sample in the same predetermined three-dimensional position in space (x-, y-, and z-co-ordinates), that is relative to the irradiation source beam(s) and detector(s). In this way a high measurement rate, i.e. samples per time unit, is secured.

Further, the same sample presentation system can be used in both at-line and on-line measurement applications.

In a preferred embodiment optical measurement is carried out on the samples. The present invention has the advantage of using at least one two-piece means for fixing each sample in at least one predetermined analysing position and thus the same effective optical aperture will be used in all measurements.

The invention is described in greater detail below with reference to the accompanying drawings which illustrate the preferred embodiments.

Description of the drawings

Fig. 1 shows a schematic drawing illustrating the way of a sample through different parts connected to an analysing equipment.

Fig. 2 illustrates the sample presentation unit connected to an on-line sample receiver.

Fig. 3 shows the sample presentation unit connected to an at-line sample receiver

Fig. 4 shows the sample presentation unit according to Fig. 3 but with some parts removed for clarity.

Fig. 5 illustrates the movements of a two-piece sample holder according to preferred embodiment.

Fig. 6 shows a top view of the two-piece sample holder according to Fig. 5 and possible beam paths.

Fig. 7 illustrates the movements of a two-piece sample compartment according to another embodiment.

Fig. 8 shows an exploded view of the at-line sample receiver.

Description of preferred embodiments

Referring now to Fig. 1 wherein a pharmaceutical sample of a solid dosage form, for example a tablet, reaches a sample-receiving unit (2) for further transport to a sample presentation unit (1). The sample receiver transports and arranges the samples for sequential queuing and feeds samples to the sample presentation unit. The object of the presentation unit is to present the sample to an analysing equipment (4) so that a measurement(s) can be carried out on the sample. When the measurements for the analyses are completed the sample is ejected from the sample presentation unit.

In a preferred embodiment the sample receiver (2) is connected on-line for example to a tabletting process. In the embodiment shown in Fig. 2, a transport line (2a) from the tabletting process represents the sample receiver (2). The transport line is connected to a transport slot (21) on the sample presentation unit (1).

In another embodiment shown in Fig. 3 the sample presentation unit (1) is arranged for use at-line and thus for receiving samples from a batch source, for example samples withdrawn from a tabletting process. The at-line sample receiver (2b) will be described in detail below with references to Fig. 8.

The analyses of the samples take place in a predetermined analysing position in the sample presentation unit wherein a sample is temporarily fixed while the measurement is performed. A two-piece means for fixing comprising a first and a second sample holding part encloses the sample in the analysing position.

In Fig. 4, 5 and 6 a preferred embodiment of two-piece means for fixing (9) is illustrated.

In another embodiment shown in Fig. 7, the two-piece means for fixing (39) are designed to constitute a closed compartment having a fixed volume around the sample (14). This embodiment is applicable for measurements using microwave radiation and detection. The predetermined volume is set to fit the frequency of radiation used in the measurements. A microwave source (37) is positioned in one the sample holding compartments (39a, 39b).

The sample presentation unit (1) is illustrated in Fig. 4 wherein some parts have been taken away for clarity. The sample presentation unit (1) comprises a wheel (3) for pre-alignment of samples and their transport to a predetermined analysing position (6). The samples are transported as the wheel rotates about its central axis. The wheel (3) is connected to a stepping motor (8) and the rotation is performed in discrete steps. At the analysing position (6), the two-piece means of fixing (9, 39) encloses the sample (14) and secures that a plurality of samples are sequentially presented to the analysing equipment in a precise and standardised three-dimensional position. The two-piece means (9, 39) comprises a first (9a, 39a) and a second (9b, 39b) sample holding part. The two parts are movable between a resting position wherein a sample, such as a tablet, is provided for analyse and a fixing position wherein the tablet is analysed.

On the circumference of the wheel (3) there is at least one hole provided for receiving samples and to act as pre-alignment (13) for a sample prior to being subjected to the predetermined analysing position (6). Each hole is lined with an elastic seal (15) that seals against the outer periphery of the sample and contributes to minimise stray radiation. Further, the elastic seal (15) keeps the sample in the pre-alignment means (13) so that each sample is presented to the two-piece sample holder (9, 39) with a pre-determined orientation relative to the beam path. As the wheel (3) rotates in discrete steps to present a sample to the analysing position (6), each pre-alignment means (13) passes three different positions within the sample presentation unit (1):

1) a sample receiving position (5),
2) the analysing position (6), and
3) a sample ejecting position (7).

The three positions are illustrated in Fig. 4.

Samples are provided from a transport slot (21) to the sample receiving position (5) and one sample at a time is then inserted into the pre-alignment means (13) by pneumatic loading means (12).

At the analysing position (6) the sample is temporarily fixed between a first and a second sample holding part (9a, 9b, 39a, 39b). In a preferred embodiment the sample holding parts each has an aperture (20) to define a beam path (16) through the sample subjected to an optical measurement.

In the ejecting position (7) the sample is ejected by pneumatic ejecting means (11). The empty pre-alignment means (13) now proceeds to receive a new sample.

Referring now to Fig. 5 and 6, the sample fixing means comprises first (9a) and a second (9b) sample holding parts. In this preferred embodiment for performing an optical measurement, the two parts (9a, 9b) each have an aperture (20) so as to expose each side of the sample to the measuring beam(s). By means of the pre-alignment means (13) in the

wheel (3), the sample now has reached its final alignment relative to a measurement optical axis(es) at the analysing position (6). Each tablet holding part (9a, 9b) is movable by pneumatic means (10).

At the analysing position (6), a sample is temporarily fixed between the first (9a, 39a) and the second (9b, 39b) sample holding parts. The sample holding parts each has an aperture (20) that, when enclosing a sample (14), together constitutes the effective optical aperture (22) for the measurement(s). That is, when the holders are joined and firmly enclose the sample snugly, they define the delimited beam path (16) for radiation through the sample (14) that is subjected to the optical measurement(s). In Fig. 6 the analysing equipment (4) is schematically shown as dark circles illustrating radiation source(s) (17), detector(s) (18) and/or camera(s) (19). In this way the same effective aperture (22) is used for all samples to be analysed, whereby the precision is significantly improved compared with known prior art.

Reference is now made to Fig. 5 or Fig. 7 of the drawings. The first (9a, 39a) and second (9b, 39b) sample holding parts are adapted to move between a fixing position (II) and a resting position (I, III). When the two parts are moved towards each other to enclose an intermediate sample (14), they are moved into the fixing position (II). In this position the measurement takes place. After the measurement, the two parts are moved away from each other to release the sample. The sample holding parts are thus moved into the resting position. As the two sample holding parts move away from each other the wheel (3) is stepped forward to present a new sample to be analysed in the analysing position (6). The sample, still in the pre-alignment means (13), continues with the wheel to the ejecting position (7) where the sample is ejected.

Preferably, the optical measurement is performed by means of near-infrared (NIR) spectrometry and/or a spectrometric method based on Raman scattering and/or a spectrometric method based on absorption in the UV, visible, or infra-red (IR) wavelength region, or luminescence, such as fluorescence spectrometry, or based on X-ray. Here,

measurements can be conducted in the reflectance and/or the transmission mode. The measurement can also be performed by means of imaging using any of these spectrometric techniques. Further, measurements can also be based on microwave technology.

Reference is now made to Fig. 8 illustrating the second embodiment for the sample receiver (2). The at-line sample receiver (2b) comprises a conical shaped rotating part (42) that constitutes the bottom of an open vessel (43) with a cylindrical geometry. The vessel has a ring as a partially open top lid (41) where the open hole is located in the centre of the lid. Through the top opening (45) samples are poured into the receiver. The function of the receiver is based on that samples, for example tablets or capsules, typically have an advantageous and well-defined geometry. That is, the length, width and thickness of a specific sample type are not all identical. In this way orientation and sorting for queuing of samples can be conducted by means of centre of gravity relations and gravity. Indeed, the function of the receiver only requires that two of these sample measures are at least slightly different. Thus, the receiver will work with common types of tablet and capsule geometries.

The detailed functionality is described in the following section. From a batch source or from a production line, tablets are fed into the open top (45) lid of the at-line sample receiver. The tablets fall down alongside the rotating cone (42). Through rotation, by means of friction from the surface (46) of the cone and by gravity, samples are forced to obtain both a laying position and forced towards the outer periphery of the cone (42). Further, sorting and queuing up is accomplished through utilising a slit like opening between the surface (46) of the cone and the lower inner edge (47) of the top lid. The opening has been given a height that is adjusted to precisely fit one of a sample's geometries. In this way, samples are forced all the way down to the outermost periphery of the cylindrical vessel (43), which in turn also constitutes the base of the cone. Samples are thereby lined-up and transported to exit (44) the sample receiver device while having obtained a predetermined orientation. The exit port (44) is located at one position along the

bottom periphery of the vessel. Through the exit port (44) samples are feed into a transport slot (4) that connects the sample receiver unit (2) with the sample presentation unit (1).

Finally, it will be understood by a person skilled in the art that the present invention is not limited to the described embodiments but can be modified in many different ways within the scope of the appended claims.

CLAIMS

1. A sample presentation apparatus for use in analysing pharmaceutical samples, comprising means for feeding said samples sequentially through a sample presentation unit (1) comprising at least one predetermined analysing position (6) wherein at least one measuring radiation beam irradiates on said sample (14) when located in said analysing position characterised by at least one two-piece means (9, 39) for temporarily fixing each sample at said analysing position (6), said two-piece means comprising a first and a second sample holding part arranged at said analysing position in which said two-piece means is adapted to move between

- a resting position wherein a sample is provided for analyse, and
- a fixing position wherein a sample is analysed.

2. The apparatus according to claim 1 characterised in that said first (9a, 39a) and second (9b, 39b) sample holding parts each contact opposite surfaces of the sample (14) in the analysing position (6).

3. The apparatus according to claim 1 characterised in that said sample (14) is free from contact of the first (9a, 39a) and second (9b, 39b) sample holding parts in the resting position.

4. The apparatus according to any of claims 1-3 characterised in that said first (9a, 39a) and second (9b, 39b) sample holding parts each define a first and second aperture (20), respectively.

5. The apparatus according to claim 4 characterised in that said first and second aperture (20) together define an effective optical aperture (22) in the fixing position.

6. The apparatus according to any of the preceding claims characterised in that said first (39a) and second (39b) sample holding parts each define a first and second compartment having a predetermined volume.

7. The apparatus according to claim 1 characterised in that said means for feeding samples sequentially through an analysing position (6) is represented by a wheel (3) comprising at least one pre-alignment means (13) for receiving at least one sample (14).

8. The apparatus according to claim 7 characterised in that said pre-alignment means (13) defines at least one hole in the wheel (3) comprising an elastic seal (15) to keep the sample (14) in the pre-alignment means (13).

9. The apparatus according to claim 7 characterised in that said samples (14) reach the wheel (3) through a sample receiver (2).

10. The apparatus according to claim 9 characterised in that said sample receiver (2) is a transport line (2a) connected on-line to a tabletting process to for providing said pre-alignment means (13) with samples (14).

11. The apparatus according to claim 9 characterised in that said sample receiver (2) is an at-line sample receiver (2b) for providing said pre-alignment means (13) with samples (14) from a batch source.

12. The apparatus according to any of claims 1-11 characterised in that said sample (14) is a solid dosage form such as a tablet, a pellet or a capsule.

13. A sample receiver arranged at an apparatus according to claim 1 for receiving samples from a batch source characterised by a conical shaped rotating part (42) that constitutes a bottom of an open vessel (43) with a cylindrical geometry.

14. A sample receiver according to claim 13 characterised in that said conical part (42) defines a surface (46) comprising means for friction.

15. A sample receiver according to claim 13 characterised in that said open vessel (43) has a partially open top lid (41) defining a top opening (45) for receiving samples.

16. A sample receiver according to claim 13 characterised in that a slit like opening wherein samples are lined-up is formed between the surface (46) of the conical part (42) and the lower inner edge (47) of the open vessel (41).

17. A sample receiver according to claim 13 characterised in that said open vessel (43) defines an exit port (44) at one position along its bottom periphery through which samples exit the sample receiver.

18. A method for presenting pharmaceutical samples to a sample presentation unit comprising the following steps:

- receiving a sample in a receiving position (5) of the sample presentation unit from a receiver unit (2);
- feeding said sample sequentially through said sample presentation unit (1) comprising at least one predetermined analysing position (6);
- temporarily fixing said sample (14) at the analysing position (6) by a two-piece fixing means (9, 39) comprising a first and a second sample holding part in a fixing position;
- moving said first and second sample holding parts to a resting position wherein the sample is transported to an ejecting position (7).

19. A method according to claim 18 wherein the sample (14) is irradiated with at least one measuring radiation beam (16) during said temporarily fixing in the analysing position (6) to perform a measurement on the sample.

20. A method according to claim 19 wherein said measurement is an optical measurement.

21. A method according to claim 20 wherein said optical measurement is carried out by means of near-infrared (NIR) spectrometry and/or a spectrometric method based on Raman scattering and/or a spectrometric method based on absorption in the UV, visible, or infra-red (IR) wavelength region, or luminescence, such as fluorescence spectrometry, or based on X-ray.

22. A method according to claim 20 wherein said optical measurement is carried out by means of near-infrared (NIR) spectrometric imaging and/or a spectrometric imaging method based on Raman scattering and/or a spectrometric imaging method based on absorption in the UV, visible, or infra-red (IR) wavelength region, or luminescence, such as fluorescence spectrometric imaging, or based on X-ray.

23. A method according to claim 19 wherein the irradiation of the sample (14) is carried out by microwaves.

24. Use of a sample presentation apparatus (1) for analysing a pharmaceutical product wherein the sample presentation apparatus is constructed according to any of claims 1-12.

25. Use of a sample receiver (2a) according to any of claims 13-17 for receiving pharmaceutical products to be analysed.

ABSTRACT

The present invention relates to a sample presentation apparatus for use in analysing equipment for pharmaceutical products, for example solid dosage forms such as a tablet, a pellet or a capsule. The invention further relates to a method for presentation of samples to the analysing equipment. Samples are sequentially fed through a sample presentation unit (1) comprising at least one predetermined analysing position (6) wherein at least one measuring radiation beam irradiates on the sample (14) when located in the analysing position characterised by at least one two-piece means (9, 39) for temporarily fixing each sample at said analysing position (6), the two-piece means comprises a first and a second sample holding part arranged at the analysing position in which the two-piece means is adapted to move between

- a resting position wherein a sample is provided for analyse, and
- a fixing position wherein a sample is analysed.

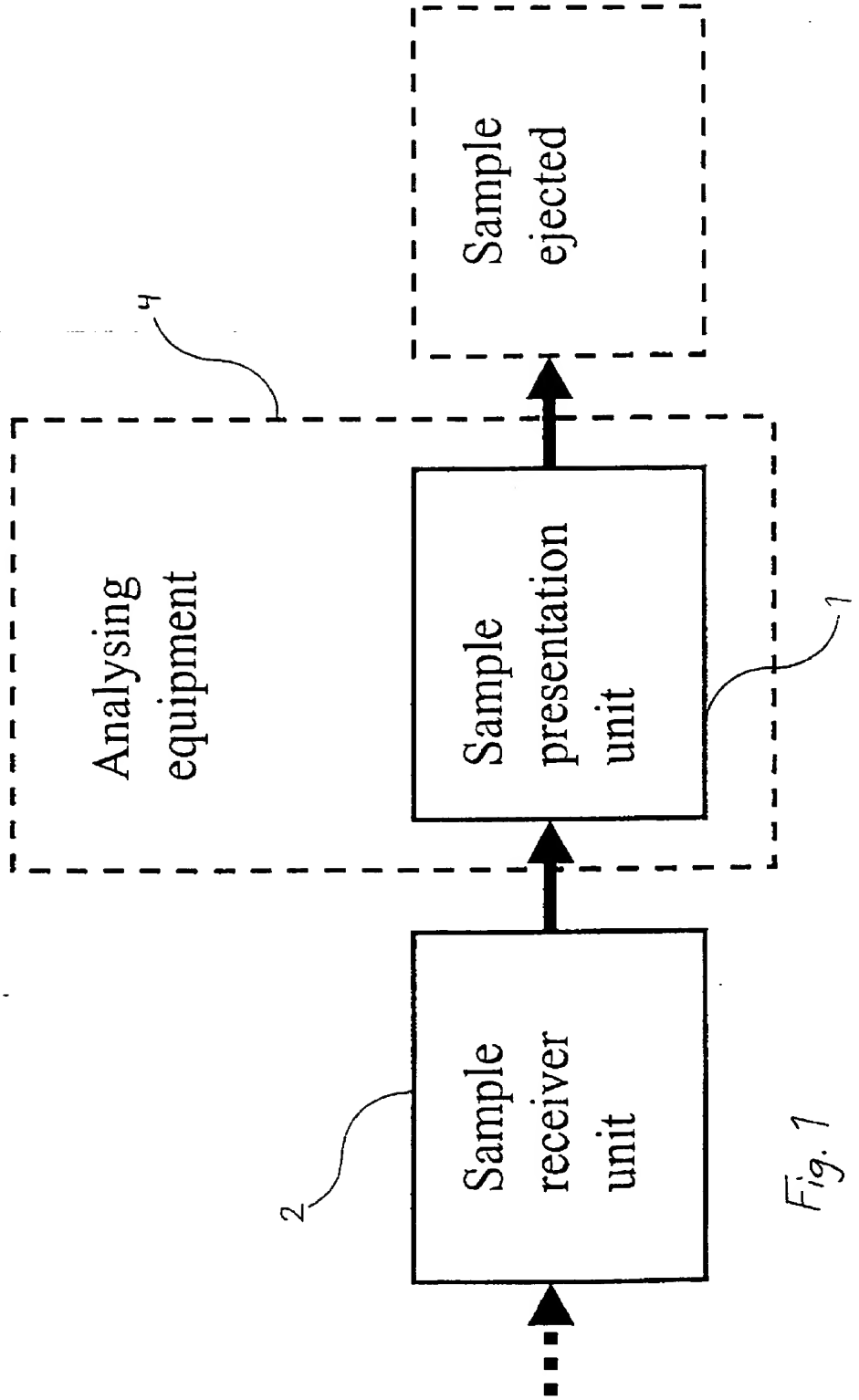
Sample ejected
4
Analysing equipment
Sample presentation unit
1
Sample receiver unit
2

Fig. 1

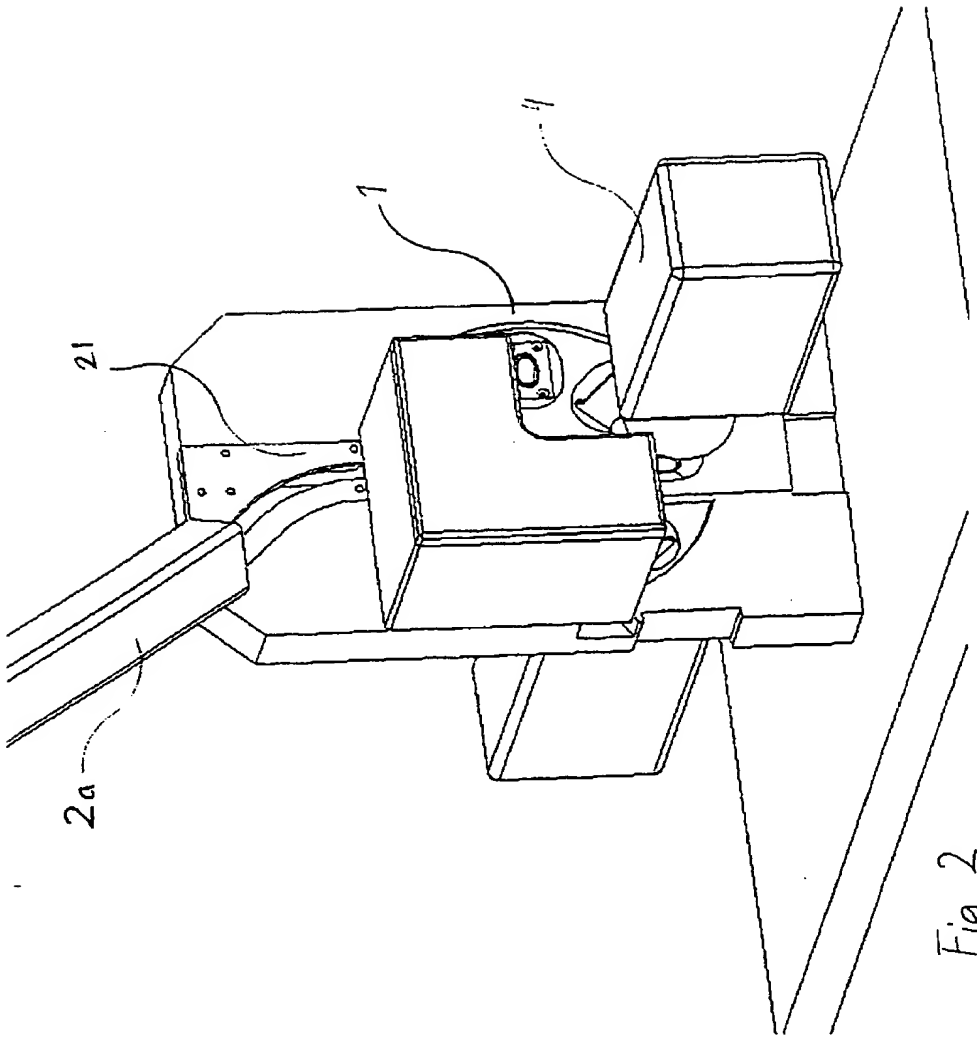

Fig 2

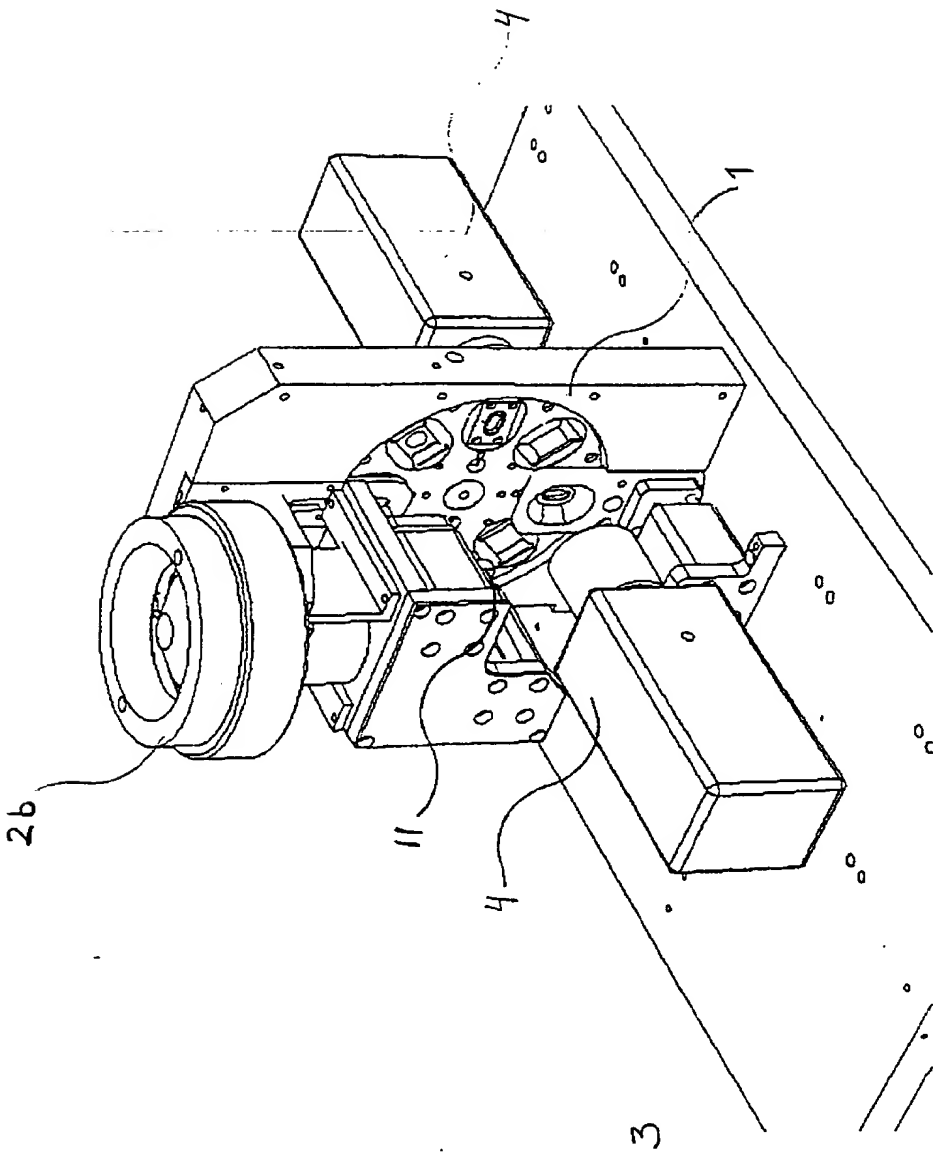

Fig. 3

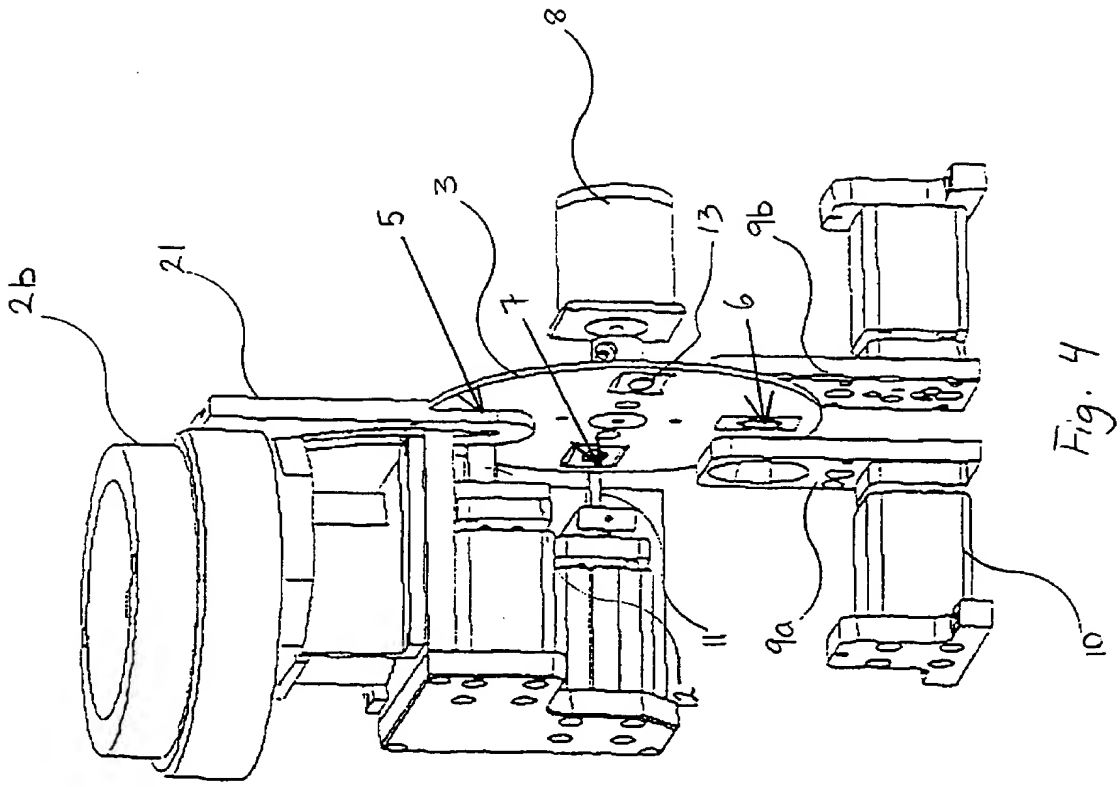

Fig. 4

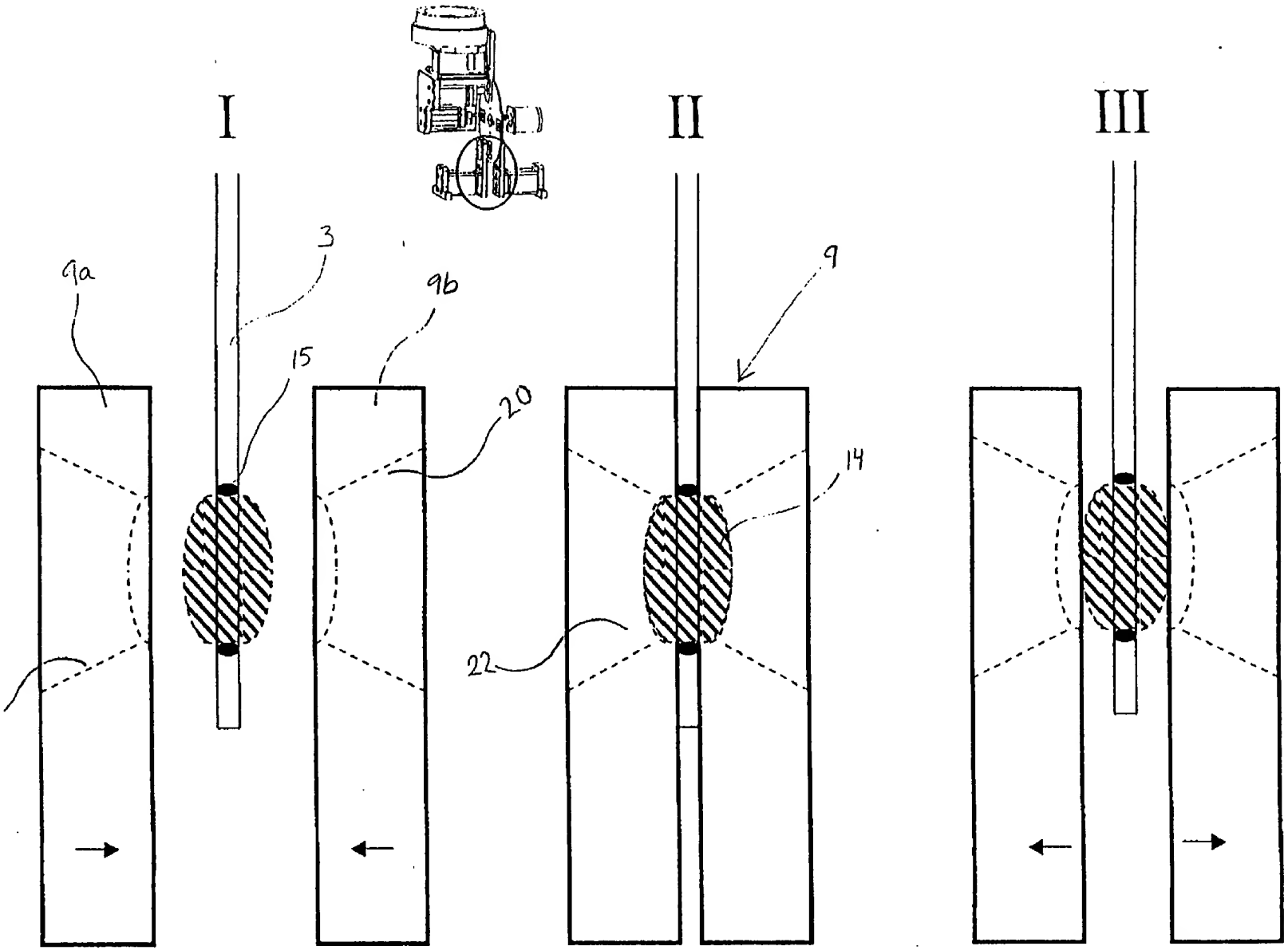

Fig. 5

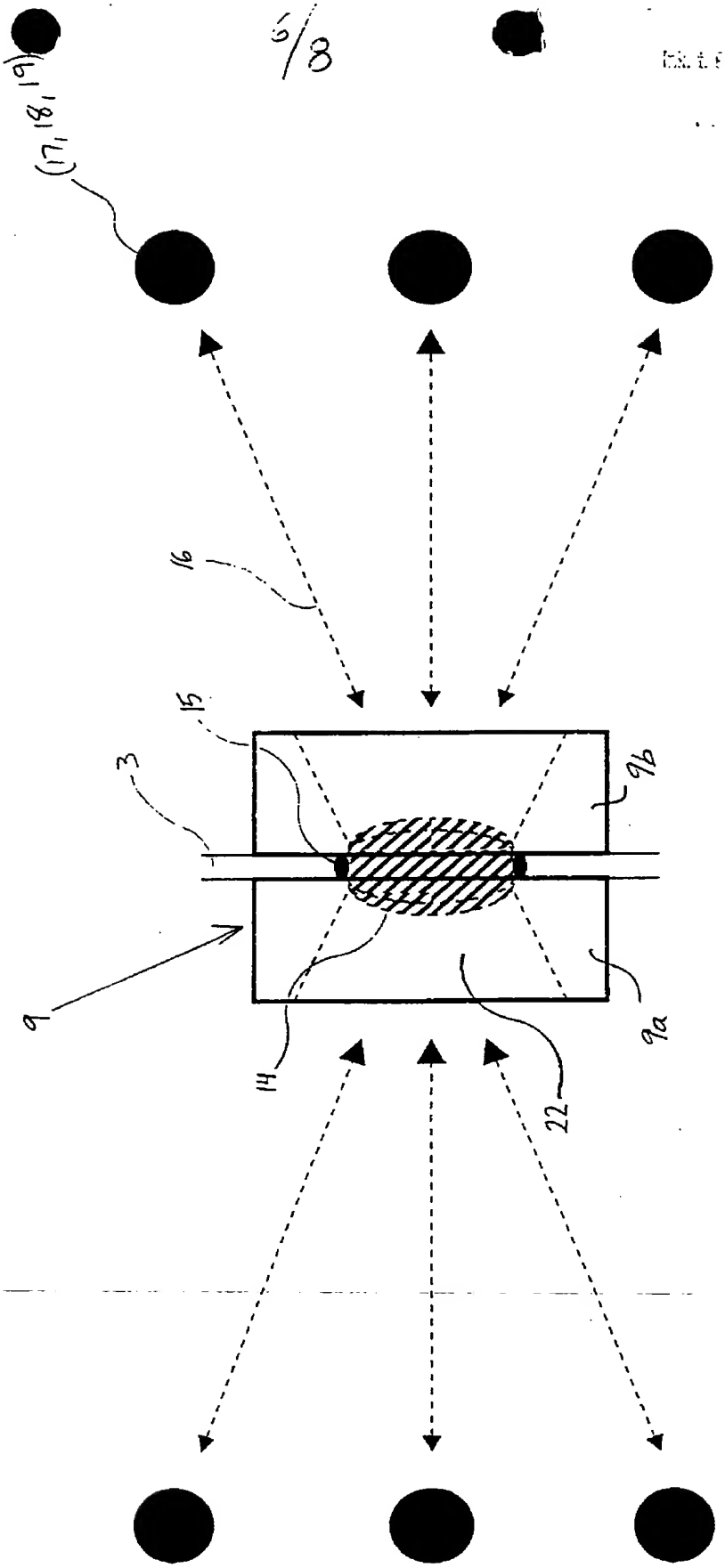

Fig. 6

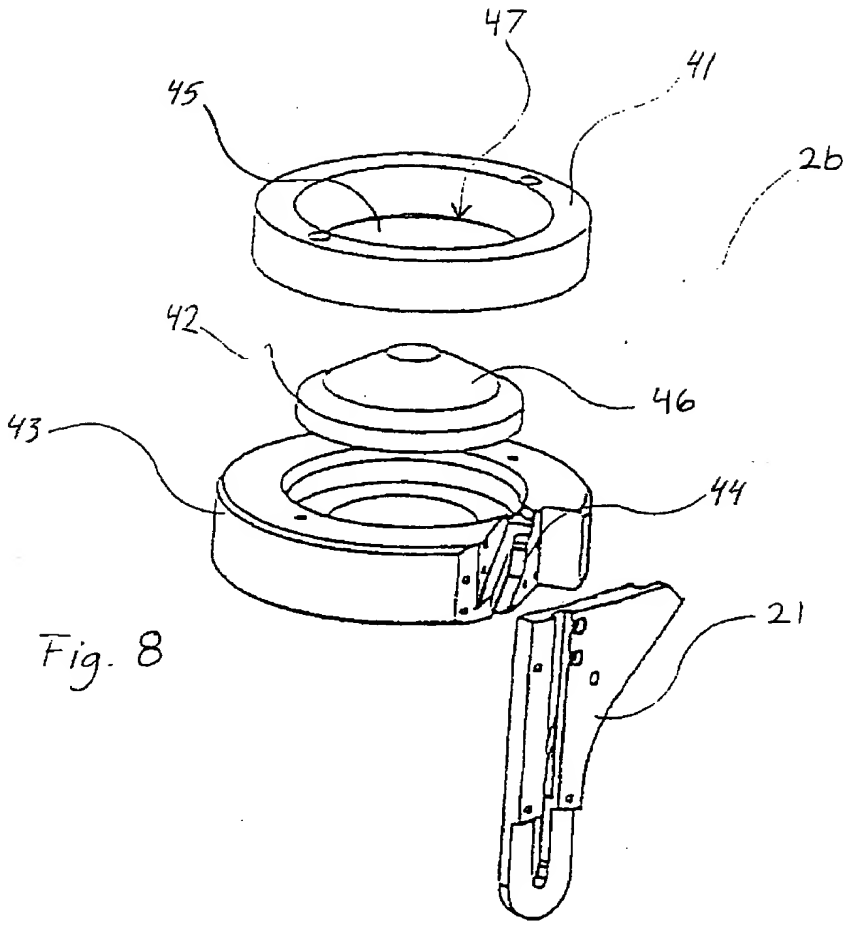

Fig. 8

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference *(if desired) (12 characters maximum)* A2236-1 WO

Box No. I TITLE OF INVENTION

APPARATUS AND METHOD FOR ANALYSING

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This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

☒ Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

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- ☒ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

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- ☐ all designated States except the United States of America
- ☒ the United States of America only
- ☐ the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

ÖSTLING, Göran
AstraZeneca Tablet Production, Sweden
S-151 85 Södertälje
Sweden

This person is:
- ☐ applicant only
- ☒ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: SE

State *(that is, country)* of residence: SE

This person is applicant for the purposes of:
- ☐ all designated States
- ☐ all designated States except the United States of America
- ☒ the United States of America only
- ☐ the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

This person is:
- ☐ applicant only
- ☐ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of:
- ☐ all designated States
- ☐ all designated States except the United States of America
- ☐ the United States of America only
- ☐ the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

This person is:
- ☐ applicant only
- ☐ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of:
- ☐ all designated States
- ☐ all designated States except the United States of America
- ☐ the United States of America only
- ☐ the States indicated in the Supplemental Box

☐ Further applicants and/or (further) inventors are indicated on another continuation sheet.

Box No.V DESIGNATION OF STATES

The following designations are hereby made under Rule 4.9(a) *(mark the applicable check-boxes; at least one must be marked)*:

Regional Patent

- [x] **AP** **ARIPO Patent:** **GH** Ghana, **GM** Gambia, **KE** Kenya, **LS** Lesotho, **MW** Malawi, **MZ** Mozambique, **SD** Sudan, **SL** Sierra Leone, **SZ** Swaziland, **TZ** United Republic of Tanzania, **UG** Uganda, **ZW** Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- [x] **EA** **Eurasian Patent:** **AM** Armenia, **AZ** Azerbaijan, **BY** Belarus, **KG** Kyrgyzstan, **KZ** Kazakhstan, **MD** Republic of Moldova, **RU** Russian Federation, **TJ** Tajikistan, **TM** Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- [x] **EP** **European Patent:** **AT** Austria, **BE** Belgium, **CH and LI** Switzerland and Liechtenstein, **CY** Cyprus, **DE** Germany, **DK** Denmark, **ES** Spain, **FI** Finland, **FR** France, **GB** United Kingdom, **GR** Greece, **IE** Ireland, **IT** Italy, **LU** Luxembourg, **MC** Monaco, **NL** Netherlands, **PT** Portugal, **SE** Sweden, **TR** Turkey, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- [x] **OA** **OAPI Patent:** **BF** Burkina Faso, **BJ** Benin, **CF** Central African Republic, **CG** Congo, **CI** Côte d'Ivoire, **CM** Cameroon, **GA** Gabon, **GN** Guinea, **GW** Guinea-Bissau, **ML** Mali, **MR** Mauritania, **NE** Niger, **SN** Senegal, **TD** Chad, **TG** Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT *(if other kind of protection or treatment desired, specify on dotted line)* .....

National Patent *(if other kind of protection or treatment desired, specify on dotted line)*:

- [x] **AE** United Arab Emirates
- [x] **AG** Antigua and Barbuda
- [x] **AL** Albania .....
- [x] **AM** Armenia .....
- [x] **AT** Austria .....
- [x] **AU** Australia .....
- [x] **AZ** Azerbaijan
- [x] **BA** Bosnia and Herzegovina .....
- [x] **BB** Barbados
- [x] **BG** Bulgaria .....
- [x] **BR** Brazil .....
- [x] **BY** Belarus .....
- [x] **BZ** Belize .....
- [x] **CA** Canada
- [x] **CH and LI** Switzerland and Liechtenstein
- [x] **CN** China .....
- [x] **CR** Costa Rica .....
- [x] **CU** Cuba .....
- [x] **CZ** Czech Republic .....
- [x] **DE** Germany .....
- [x] **DK** Denmark .....
- [x] **DM** Dominica
- [x] **DZ** Algeria .....
- [x] **EE** Estonia .....
- [x] **ES** Spain .....
- [x] **FI** Finland .....
- [x] **GB** United Kingdom
- [x] **GD** Grenada
- [x] **GE** Georgia .....
- [x] **GH** Ghana .....
- [x] **GM** Gambia
- [x] **HR** Croatia .....
- [x] **HU** Hungary .....
- [x] **ID** Indonesia
- [x] **IL** Israel .....
- [x] **IN** India .....
- [x] **IS** Iceland
- [x] **JP** Japan .....
- [x] **KE** Kenya .....
- [x] **KG** Kyrgyzstan .....
- [x] **KP** Democratic People's Republic of Korea .....
- [x] **KR** Republic of Korea .....
- [x] **KZ** Kazakhstan .....
- [x] **LC** Saint Lucia
- [x] **LK** Sri Lanka
- [x] **LR** Liberia
- [x] **LS** Lesotho .....
- [x] **LT** Lithuania
- [x] **LU** Luxembourg
- [x] **LV** Latvia
- [x] **MA** Morocco .....
- [x] **MD** Republic of Moldova .....
- [x] **MG** Madagascar .....
- [x] **MK** The former Yugoslav Republic of Macedonia .....
- [x] **MN** Mongolia
- [x] **MW** Malawi .....
- [x] **MX** Mexico .....
- [x] **MZ** Mozambique
- [x] **NO** Norway
- [x] **NZ** New Zealand .....
- [x] **PL** Poland .....
- [x] **PT** Portugal .....
- [x] **RO** Romania
- [x] **RU** Russian Federation .....
- [x] **SD** Sudan
- [x] **SE** Sweden
- [x] **SG** Singapore
- [x] **SI** Slovenia .....
- [x] **SK** Slovakia .....
- [x] **SL** Sierra Leone .....
- [x] **TJ** Tajikistan .....
- [x] **TM** Turkmenistan .....
- [x] **TR** Turkey .....
- [x] **TT** Trinidad and Tobago .....
- [x] **TZ** United Republic of Tanzania
- [x] **UA** Ukraine .....
- [x] **UG** Uganda .....
- [x] **US** United States of America .....
- [x] **UZ** Uzbekistan .....
- [x] **VN** Viet Nam .....
- [x] **YU** Yugoslavia .....
- [x] **ZA** South Africa .....
- [x] **ZW** Zimbabwe .....

Check-box reserved for designating States which have become party to the PCT after issuance of this sheet:

- [ ] .....

Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. *(Confirmation (including fees) must reach the receiving Office within the 15-month time limit.)*

Box No. VI PRIORITY CLAIM ☐ Further priority claims are indicated in the Supplemental Box.

Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is: national application: country	regional application:* regional Office	international application: receiving Office
item (1) 31.01.2000 (31 Jan 2000)	0000314-5	Sweden (SE)		
item (2)				
item (3)				

☒ The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) *(only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office)* identified above as item(s): (1)

** Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.*

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA) *(if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used)* :

ISA / SE

Request to use results of earlier search; reference to that search *(if an earlier search has been carried out by or requested from the International Searching Authority):*

Date *(day/month/year)*	Number	Country *(or regional Office)*
06 October 2000	SE00/00079	Sweden

Box No. VIII CHECK LIST; LANGUAGE OF FILING

This international application contains the following **number of sheets:**

request	: 4
description (excluding sequence listing part)	: 13
claims	: 4
abstract	: 1
drawings	: 11
sequence listing part of description	:
Total number of sheets	: 33

This international application is **accompanied by** the item(s) marked below:

1. ☒ fee calculation sheet
2. ☐ separate signed power of attorney
3. ☒ copy of general power of attorney; reference number, if any: GF53/2001/ÅD
4. ☐ statement explaining lack of signature
5. ☐ priority document(s) identified in Box No. VI as item(s):
6. ☐ translation of international application into (language):
7. ☐ separate indications concerning deposited microorganism or other biological material
8. ☐ nucleotide and/or amino acid sequence listing in computer readable form
9. ☒ other *(specify)*: ITS Report SE00/00079

Figure of the drawings which should accompany the abstract: 1

Language of filing of the international application: English

Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).

Södertälje, 26 January 2001

Eva Selin

Eva Selin
Global Intellectual Property, AstraZeneca AB

For receiving Office use only

1. Date of actual receipt of the purported international application:	2. Drawings: ☐ received: ☐ not received:
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:	
4. Date of timely receipt of the required corrections under PCT Article 11(2):	
5. International Searching Authority (if two or more are competent): ISA /	6. ☐ Transmittal of search copy delayed until search fee is paid.

For International Bureau use only

Date of receipt of the record copy by the International Bureau:

Applicant: **AstraZeneca AB**
S-151 85 Södertälje
Sweden

Title: **APPARATUS AND METHOD FOR ANALYSING**

Reference: A2236-1 WO

Inventors: Staffan Folestad
Kurt Lundström
Göran Östling